Journal of the American College of Cardiology Vol. 54, No. 25, 2009

Published by Elsevier Inc.

ISSN 0735-1097/09/$36.00
doi:10.1016/j.jacc.2009.10.013

QUARTERLY FOCUS ISSUE: PREVENTION/OUTCOMES

Year in Cardiology Series

The Year in Epidemiology, Health Services Research, and Outcomes Research

Mark A. Hlatky, MD,* Paul Heidenreich, MD†

Stanford and Palo Alto, California

In this paper, we summarize a few of the highlights in the fields of epidemiology, health services research, and outcomes research published between roughly April 2008 and June 2009. Our overview is necessarily selective, because the sheer number of articles published in these areas over the past year is too large to cover within the available space. Consequently, some excellent research in these fields might not be mentioned.

Epidemiology

The relationship of obesity to cardiovascular risk has been difficult to untangle, because obesity is strongly associated with several classical cardiovascular risk factors. Consequently, the role of obesity per se—as opposed to its known adverse effects on blood pressure, lipids, and diabetes—has been controversial. Several articles in the past year suggest that obesity does indeed exert an independent effect on cardiovascular risk. Perhaps the most definitive examination of the effects of obesity on health is an analysis of data from 894,576 healthy individuals drawn from 57 prospective cohort studies (1). This study showed a strong "U-shaped" relation between body mass index and all-cause mortality, with lowest mortality among participants with a body mass index between 22.5 and 25.0 kg/m^2. Most of the excess mortality due to obesity was caused by cardiovascular disease, particularly among younger participants. A prospective study of 54,783 Danes showed the cardiovascular risk of obesity was independent of traditional cardiac risk factors and several behavioral risk factors, including physical activity (2); the Framingham Offspring Study of 4,780 adults showed a similar result (3). An analysis of the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American College of Cardiology/American Heart Association Guidelines) registry demonstrated that the age of first myocardial infarction (MI) was inversely proportional to body mass index (i.e., obese subjects had heart attacks at younger ages) (4). These studies underscore the important adverse effects of obesity on cardiovascular disease.

Genome-wide association studies have become more feasible with the commercial availability of "gene chips" containing a very large number of genetic markers. The association of cardiovascular disease with a marker at chromosome 9p21.3 was further confirmed by the Cardiogenics Consortium of 7 case-control studies (5). However, the Women's Genome Health Study found little clinical value in genotyping at chromosome 9p21.3. Despite having a significant and independent association with incident cardiovascular disease, 9p21.3 did not improve risk prediction, as assessed either by the c-index or by newer risk reclassification measures (6).

A large genome-wide association study of stroke reported that a locus at 12p13 was significant (7); interestingly, there was no association of the 9p21.3 marker with stroke in this study. Another genome-wide associated study reported an association between statin-induced myopathy and variants in the *SLCO1B1* gene (8), which encodes a protein involved in statin metabolism. Steady state warfarin dose levels were confirmed to be correlated with patient genotype in a large study of 4,043 patients (9), but 2 independent analyses reported that genotyping at this locus was not cost-effective (10,11). On the basis of information currently available, the value of any genetic markers of cardiovascular disease in clinical care is as yet unestablished.

Prevention

One of the biggest developments of the past year was the publication of the JUPITER (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin) trial (12). In the JUPITER trial, men age 50 years and older and women age 60 years and older with a low-density lipoprotein (LDL) cholesterol level below 120 mg/dl and a high-sensitivity C-reactive protein level above 2.0 were randomized to rosuvastatin or placebo and followed for a median of 1.9 years. Rosuvastatin therapy reduced the composite end point of confirmed cardiac

From the *Stanford University School of Medicine, Stanford, California; and the †Palo Alto Veterans Affairs Medical Center, Palo Alto, California. Dr. Heidenrich is a consultant for Boston Scientific.

Manuscript received October 20, 2009, accepted October 20, 2009.

JACC Vol. 54, No. 25, 2009
December 15/22, 2009:2343–51

death, MI, or stroke from 1.76% to 0.93%, a relative risk reduction of 47% ($p < 0.0001$). Analyses of data from the National Health and Nutrition Study suggest that between 6.5 million (13) and 8.1 million (14) individuals meet "strict" JUPITER eligibility criteria, and several million more might be eligible for statin therapy if the age or other JUPITER entry criteria were relaxed. The JUPITER results engendered some controversy about the value of expanding indications for statins therapy and about the value of high-sensitivity C-reactive protein screening.

Expansion of statin therapy to lower-risk subjects might reduce their relative risk of cardiovascular disease yet provide less absolute risk reduction than among higher-risk subjects. The cost-effectiveness of prevention therapies is generally less favorable as they are applied to lower-risk subjects. Nevertheless, 2 independent cost-effectiveness studies suggest that statin therapy might be economically attractive among lower-risk individuals (15,16). An analysis based on data from the Heart Protection Study suggested that if statin therapy cost $1/day or less, it would be cost-effective even in individuals with Framingham Risk scores below 10% (15). A model by Pletcher et al. (16) suggested that if statins cost <$1.50/day, then it would be cost-effective to treat even relatively low-risk patients for primary prevention. Both of these analyses assumed that statin therapy is well-tolerated and safe, even with long-term use. A meta-analysis of 15 randomized trials (96,840 participants) found no excess cancer risk from statin therapy, but mean follow-up was only 4.4 years (17).

Recent studies also addressed the question of the LDL level at which drug therapy should be initiated and what LDL target to use. An analysis of the JUPITER trial suggested that lower attained LDL levels were associated with better outcomes (18), but this was not a randomized comparison of LDL targets. The PROVE-IT (Pravastatin or Atorvastatin Evaluation and Infection Therapy) trial of different treatment intensities found that baseline LDL levels modified the efficacy of intensive statin therapy compared with less-intensive statin therapy, such that only patients with higher pre-treatment LDL levels benefitted, and patients with lower baseline LDL levels (especially <80 mg/dl) obtained no additional benefit (19).

Outcomes

The comparison of outcomes after drug-eluting stent (DES) or bare-metal stent (BMS) implantation was a vibrant cottage industry over the past year, with multiple studies that reported on the basis of various clinical and administrative datasets (20–28) (Table 1). Most studies examined data after the approval and marketing of DES (April 2003 in the U.S.), but a few studies compared outcomes before and after DES became available (22,25). Because of the very rapid adoption of the DES, there was a

Table 1 Comparison of Outcomes After DES or BMS in Various Clinical and Administrative Datasets

Author, Ref. #	Study/ Population	Date Start	Date End	Follow-Up, yrs	Patients, n	DES, %	Database Type	Statistical Method	HR for Death (DES/BMS)	95% CI	HR for Death/MI	95% CI	Late Hazard
Mauri et al. (20)	Massachusetts	April 2003	September 2004	2.0	17,793	65	Clinical	PS matching	0.82	0.73–0.92	0.81	0.71–0.92	Yes
Austin et al. (21)	Scotland	January 2003	September 2005	2.0	7,499	15	Clinical	PS matching	0.63	0.40–0.99	1.02	0.69–1.54	No
Ryan et al. (22)	Medicare	January 2001	December 2004	2.0	22,016	42	Admin	Cox, era	0.89	0.82–0.96	0.72	0.66–0.79	NR
James et al. (23)	Swedish Registry	January 2003	December 2006	2.7	47,967	41	Clinical	PS adjustment	0.94	0.85–1.05	0.96	0.89–1.03	Yes
Groeneveld et al. (24)	Medicare	April 2003	December 2003	2.0	143,930	50	Admin	PS matching	0.83	0.81–0.86	0.80	0.78–0.83	No
Hannan et al. (25)	New York State	October 2002	March 2004	2.0	24,372	39	Clinical	Cox, era	0.94	0.84–1.04	0.90	0.83–0.97	No
Douglas et al. (26)	NCDR/Medicare	January 2004	December 2006	2.5	262,700	83	Clinical	PS adjustment	0.75	0.72–0.79	0.75	0.72–0.79	Yes
Shishehbor et al. (27)	Cleveland Clinic	March 2003	June 2007	4.5	8,032	75	Clinical	PS matching	0.54	0.45–0.66	NR	NR	NR
Kaltoft et al. (28)	Western Denmark	January 2002	June 2005	2.0	12,395	28	Clinical	Cox PH	0.97	0.83–1.13	1.24	1.02–1.51	Yes

BMS = bare-metal stent(s); CI = confidence interval; DES = drug-eluting stent(s); HR = hazard ratio; MI = myocardial infarction; NCDR = National Cardiovascular Data Registry; NR = not reported; PH = proportional hazard; PS = propensity score.

strong selection bias for DES over BMS, with differences in many measured clinical characteristics and presumably many differences in unmeasured characteristics, such as likely adherence to antiplatelet therapy. Most studies used propensity score methods to control for selection bias evident from measured clinical characteristics. These studies generally found lower risk for total mortality, the composite end point of death or MI, and MI alone for patients who received DES compared with patients who received BMS (Table 1). Some, but not all, of these studies also found an increased risk of MI in later follow-up. However, none of these studies controlled for concomitant drug therapy in general or for clopidogrel use in particular. A meta-analysis of randomized trials and observational studies (29) found that the DES/BMS hazard ratio for all-cause mortality was 0.97 (95% confidence interval: 0.81 to 1.15) on the basis of 21 randomized trials and 0.77 (95% confidence interval: 0.69 to 0.85) on the basis of 22 large observational studies. It is notable that the point estimate of the DES/BMS hazard ratio derived from randomized studies (0.97) was outside the confidence limits derived from the observational studies (95% confidence interval: 0.69 to 0.85), and vice versa. So despite the relative consistency of the results of recent observational outcomes, studies showing lower mortality after DES, it is possible that this is due to consistent confounding and strong patient selection rather than a true treatment effect. This possibility is strengthened by evidence of lower mortality within 30 days of DES implantation in some studies (20,21) and reports of fewer admissions for bleeding after DES (26), despite more intensive antiplatelet therapy.

Economic and Quality-of-Life Outcomes

The economic effects of clinical management strategies have drawn increased scrutiny and have been evaluated in both randomized trials and simulation studies. The cost-effectiveness of percutaneous coronary intervention (PCI) compared with optimal medical therapy for patients with stable angina was prospectively assessed in the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive drug Evaluation) trial (30). Medical costs were higher over 3 years among patients randomized to PCI ($34,800 vs. $24,700), whereas survival was similar, so that the cost-effectiveness of PCI was unfavorable ($168,000/quality adjusted life-year [QALY] added). The cost-effectiveness of therapeutic hypothermia after cardiac arrest was evaluated in a simulation model by Merchant et al. (31), who estimate that patients treated with hypothermia gained 0.66 QALYs of survival at a net cost of $31,300, which implies a favorable cost-effectiveness ratio of $47,200/QALY added. Nurse-led management of heart failure was evaluated in a randomized trial of 406 patients who lived in Harlem (32). The cost of the intervention ($2,200/patient) was largely offset by reduced hospital stays ($2,400/patient), so the net medical costs were not significantly different. The intervention patients had better quality of life, so the cost-effectiveness of the program was favorable (<$16,000/QALY).

Improvement of patient quality of life is an important goal of medical management and hence has been assessed in randomized trials. Percutaneous coronary intervention improved quality of life significantly compared with medical therapy for up to 24 months in the COURAGE trial (33). Percutaneous coronary intervention to open occluded coronary arteries late after an acute myocardial infarction (AMI) improved patient quality of life at 4 months but not in longer follow-up in the OAT (Occluded Artery Trial) (34). Implantable cardioverter-defibrillator (ICD) therapy did not affect quality of life either for the better or the worse in the SCD-HEFT (Sudden Cardiac Death in Heart Failure Trial) (35). Surgical ventricular reconstruction surgery did not improve quality of life when compared with coronary artery bypass graft surgery (CABG) in the STICH (Surgical Treatment of Ischemic Heart Failure) randomized trial and was significantly more costly (36).

Financial Incentives

Economic incentives are designed to alter the behavior of patients and physicians. Some recent studies show that even relatively small amounts of money might be surprisingly influential. Doshi et al. (37) used data from the Philadelphia VA Medical Center to assess the effect of increasing copayments for prescription drugs from $2 to $7. Adherence to statins dropped much more among patients whose copayments were increased (−19% vs. −12%), and they were 2 to 3 times as likely to have a prolonged gap in statin use. Although the copayment was relatively small, it had a large impact upon the behavior of these low-income patients. Solomon et al. (38) found a similar effect of copayments on the use of pharmacotherapy among patients with newly diagnosed hypertension, hyperlipidemia, or diabetes.

Some of the most intriguing data on the effect of financial incentives on behavior came from a workplace program in which smokers were randomized to receive $100 for completing a smoking cessation program, an additional $250 for proven abstinence within the first 6 months, and $400 more for an additional 6 months of abstinence. Smoking cessation was significantly greater at 1 year (15% vs. 5%, $p < 0.001$) in the group given financial incentives (39).

Pay-for-performance programs have been used to encourage physicians to improve the quality of care, particularly in the United Kingdom. The potential of these programs to exacerbate disparities has been a concern, but recent data on the delivery of primary care services suggests that general practitioners in relatively poor areas increased quality of care to a greater extent than more well-to-do areas and narrowed the gap in quality measures among regions (40).

Health Policy

Clinical practice guidelines aim to improve the quality of health care and should ideally be based on evidence rather than the opinions of experts. Several years ago, the American College of Cardiology/American Heart Association (ACC/AHA) joint practice guidelines began to grade the level of evidence supporting their practice recommendations. A recent analysis (41) demonstrated that, despite the large number of clinical trials conducted in cardiovascular medicine, ACC/AHA Class I recommendations were twice as likely to be based on expert opinion (37%) than on strong evidence from multiple randomized trials (19%). This study suggests that our current system of clinical trials, which relies mostly on industry-funded studies, does not provide the evidence most needed to guide clinical management of common cardiovascular conditions.

Coronary bypass surgery, one of the most common major procedures in the U.S., has been a prominent focus of many health policy studies. Despite concerns about overuse of CABG, most (87%) bypass surgery in Northern New England in 2004 and 2005 was found to be appropriate, meeting Class I indications from the ACC/AHA guidelines (42). The quality of care for CABG has been assessed with a variety of measures. Among 114,233 Medicare patients who were discharged alive after CABG, each major postoperative complication increased hospital costs by 50% relative to those without complications (43). Outlier payments for CABG in Medicare, which are typically due to procedural complications, dropped substantially from 2000 to 2006 but still varied significantly across U.S. hospitals, suggesting that there is still variation in quality of care for CABG (44). Risk-adjusted procedural mortality rates have been publicly reported in several states as a way to improve quality and inform consumers, but Shahian and Normand (45) suggest that these measures are flawed when comparing hospital outcomes. Guru et al. (46) found no correlation between the risk-adjusted mortality rate and the proportion of "preventable deaths" after CABG. Process measures, such as the use of aspirin, beta-blockers, and prophylactic antibiotics, might be better predictors of CABG outcomes than procedure volume (47).

Percutaneous coronary intervention (PCI) has received somewhat less attention from health policy analysts than CABG, but this might be changing as PCI volumes continue to grow while CABG volumes decline. A report from the National Cardiovascular Data Registry (NCDR) indicates that PCI conducted at hospitals without cardiac surgery seem to be as safe as PCIs performed at hospitals with cardiac surgery programs (48); emergency CABG was infrequent in both settings. Less than 5% of NCDR PCI programs routinely monitor cardiac markers after PCI procedures (49), even though procedural MI is arguably an important measure of quality of care in this setting. Percutaneous coronary intervention procedural mortality can be assessed in all programs but is clearly a crude and insensitive measure of quality of care. Hospital mortality during primary PCI for AMI was lower in higher-volume hospitals and among higher-volume operators in New York State (50).

Adherence

Perhaps the most challenging aspect of quality-of-care improvement is patient adherence to recommended treatments. Several recent studies examined the impact on outcomes of nonadherence to evidence-based drug treatments. Ho et al. (51) found that nonadherence (proportion of days covered <80%) to cardioprotective medications was quite common: 22% for angiotensin-converting enzyme (ACE) inhibitors, 26% for statins, and 29% for beta-blockers. Better adherence to these medications was associated with better survival and fewer hospital stays for heart disease. Daskalopoulou et al. (52) examined treatment of patients with an AMI with data from general practices in the United Kingdom. Compared with patients who never used statins, those who started statin therapy or continued use after MI had significantly improved survival (odds ratio: 0.72 and 0.84, respectively), whereas those who stopped statins had worse survival (odds ratio: 1.88). A similar study from Israel by Shalev et al. (53) found that patients enrolled in a health maintenance organization who were adherent to statins (defined as ≥90% of proportion of days covered), had 45% lower mortality compared with patients who were not adherent (<10% of days covered), with a significant dose–response relationship between the proportion of days covered with statins and mortality.

The evidence is mixed as to whether adherence to recommended treatments is only associated with better outcomes or actually has a cause and effect relationship. Ho et al. (51) found that adherence to statins improved outcomes but not adherence to proton pump inhibitors or H2 antagonists. In the study by Daskalopoulou et al. (52), adherence to statins, aspirin, and proton pump inhibitors were all associated with improved survival in unadjusted analyses, but only adherence to statins was significantly associated with subsequent outcome after adjustment for patient characteristics. But, in a fascinating study by Dormuth et al. (54) from British Columbia, patients adherent to statins were more likely to seek preventive services, less likely to have drug dependency, and less likely to have automobile accidents than those nonadherent to statins, suggesting that adherence might simply identify patients with generally healthier behaviors.

Assessment of adherence is potentially important for determining the appropriate response to poorly controlled chronic diseases. In a study of VA patients with poorly controlled hypertension, providers intensified treatment approximately one-third of the time, a value that was no different for those with high and poor adherence (55). These data suggest that providers were not addressing adherence when making decisions about intensification of therapy.

Quality of Care

The process of improving quality is often separated into several steps, beginning with a description of current care, followed by determining "risk factors" for poor care, creating and implementing interventions to improve care, and finally documenting whether outcomes are actually improved. During the past year numerous studies have examined this spectrum of quality-of-care research.

Time to reperfusion has been increasingly used as a measure of quality of care for AMI. Gibson et al. (56) used National Registry of Myocardial Infarction (NRMI) data to show that the median door-to-needle time for thrombolysis decreased from 59 min in 1990 to 29 min in 2006 and that door-to-balloon (D2B) time for primary PCI decreased from 111 min in 1994 to 79 min in 2006. Mehta et al. (57) found a similar improvement in median D2B times in data from the AHA's Get With The Guidelines Program: from 108 min (in 2002) to 82 min (in 2006). Despite these improvements, only 45% of patients met the recommended D2B time of <90 min. Ting et al. (58) used data from NRMI to demonstrate that patients with long waits to presentation were less likely to receive timely reperfusion (e.g., longer door-to-needle time and lower reperfusion overall) than patients presenting early after the onset of chest pain. Dorsch et al. (59) from the United Kingdom found that direct admission to the catheterization laboratory from the ambulance improved attainment of the 90-min goal for D2B from 29% to 94%.

Increased age had an adverse effect on quality of care in several recent studies. In the GRACE (Global Registry of Acute Coronary Events) registry, patients over the age of 90 years had significantly less use of aspirin (91% vs. 97%) and beta-blockers (80% vs. 87%) (60) than patients 70 years of age or younger. A similar effect of age on drug use was found among heart failure patients, with 79% ACE inhibitor use for patients age >85 years versus 82% for age ≤65 years in the Get With The Guidelines database (61). Older patients were less likely to receive appropriate cardiac resynchronization therapy (62), as were black patients (odds ratio: 0.45; 95% confidence interval: 0.36 to 0.57), those in the Northeast U.S., and those with greater left ventricular ejection fractions. Schiele et al. (63) found increasing rates over time of recommended care for elderly patients with AMI, which explained much of the large drop in mortality for ST-segment elevation MI.

Health system factors have also been associated with quality of care in recent investigations. Patients with heart failure and "do not resuscitate" orders but without other indications that care was limited were less likely to receive an assessment of left ventricular ejection fraction, ACE inhibitors, and anticoagulation when indicated (64). Timing of hospital admission was found to affect quality of care in several studies. Patients with an AMI who arrived outside of regular working hours were less likely to receive primary PCI and had longer D2B times (65). Patients with pulmonary embolism had higher mortality when admitted over the weekend than during the work week (66). Although this might indicate poorer care during the weekend, it is difficult to completely control for differences in illness severity that might exist between those admitted during on hours and those admitted during off hours.

Although quality of care is important to patients, they might be unable to judge the quality of care they receive. Lee et al. (67) that found that patient satisfaction with their care had no relationship to guideline-recommended care for patients with AMI. Satisfied patients were more likely to be older and to have better physical function and less likely to have depression.

Specialty training might affect clinical outcomes in certain conditions. Curtis et al. (68) found that physicians without formal training in cardiology who implanted ICDs had the highest rate of procedural complications, whereas physicians with training in electrophysiology had the lowest rate of complications. Karamlou et al. (69) found that patients with congenital heart disease who were operated upon by pediatric heart surgeons (defined as those whose case mix was at least 75% pediatric heart procedures) had lower in-hospital mortality than those operated upon by other surgeons.

Several studies have evaluated interventions to improve the quality cardiac care for hospitalized patients. Hospitals enrolled in the Get With The Guidelines Stroke Program demonstrated significant improvement in 7 individual measures and 1 composite measure over 5 years (70). The improvements in stroke care were seen in all hospitals, regardless of size, geography, and teaching status. Brush et al. (71) compared a 29-hospital collaborative to improve care for AMI and heart failure with a group of control hospitals. Hospitals in the collaborative had higher quality-of-care measures than noncollaborative hospitals at study entry, but both groups improved on quality measures to a similar extent over follow-up. Piazza et al. (72) randomized attending physicians to a reminder by a staff member to use prophylaxis for venous thromboembolism; patients whose attending physician received the reminder were twice as likely to receive prophylaxis and had a nonsignificant trend toward reduced symptomatic thromboembolism.

Two reports provided insight by combining results of multiple programs. In a summary of 15 randomized trials of care-coordination for Medicare patients with chronic diseases including heart failure and coronary artery disease, Peikes et al. (73) reported that overall there was no clear cost savings from these programs. However, those programs that focused on the transition from inpatient to outpatient care and those with substantial in-person

contact with the patient were most likely to be cost-neutral and lead to care improvements. A meta-analysis by Auer et al. (74) of 14 in-hospital programs to improve secondary prevention for ischemic heart disease reported that uncontrolled studies demonstrated a much larger benefit than controlled studies. Interventions that only focused on the patient and did not impact providers or the health care system were unsuccessful. Taken together, these reports indicate that improved quality and cost savings are difficult to achieve and that the benefit and cost reduction of any one program might be overstated in studies that are not randomized.

Disparities

Racial disparities have continued to be documented over the past year. In an analysis of 20-year follow-up of the CARDIA (Coronary Artery Risk Development in Young Adults) study, Bibbins-Domingo et al. (75) found that black patients have a significantly higher incidence of heart failure before the age of 50 years (0.9% to 1.1%) than white patients (0% to 0.08%, $p < 0.0001$). Patients who developed heart failure were more likely to have prior hypertension, obesity, and reduced left ventricular dysfunction indicating potential targets for prevention and screening. Shaw et al. (76), with data from the NCDR, found that black patients and women were less likely to have significant disease at coronary angiography than white men, suggesting that physicians might be more selective in their referral of white male patients. In another study, black and Hispanic patients were more likely to be referred to cardiologists for coronary artery disease than white patients but had fewer follow-up consultations (77). Compared with white patients, black patients with coronary heart disease had lower quality of life (78), were more likely to receive evidence-based medications (79), were less likely to receive discharge instructions and tobacco counseling (79), and were less likely to be treated for depression (80). Among U.S. Medicare beneficiaries, short-term mortality for AMI decreased significantly in all racial groups but decreased faster for whites than for blacks (81). With a registry of patients with myocardial infarction, Spertus et al. (82) showed that the higher rates of mortality, repeat hospital stay, and angina and the lower quality of life for blacks compared with whites was largely explained by differences in patient characteristics and site of care. Black patients hospitalized emergently for heart failure were younger, less severely ill on admission, and less likely to experience short-term fatal and nonfatal outcomes than white patients (83).

One hypothesis for the observed poorer outcomes in black compared with white patients has been racial discrimination leading to increased stress and progression of atherosclerosis. Albert et al. (84) found in the Dallas Heart Study that black patients who reported discrimination were more likely to be college graduates, to have a family history of myocardial infarction, and to be more physically active than black patients who did not report discrimination (each $p < 0.05$). However, they found no association between reports of discrimination and aortic wall thickness, aortic plaque area, prevalent coronary artery calcification, or elevated C-reactive protein for different ethnic groups.

Sex differences have been the focus of many studies of heart disease during the past year. When compared with men, women with coronary artery disease showed similar declines in mortality (81), and women with acute coronary syndromes had fewer high-risk angiographic features, were less likely to receive aspirin or glycoprotein IIb/IIIa inhibitors, and were less often discharged on aspirin or statin (85). Women had similar in-hospital acute coronary syndrome mortality but higher rates of cardiogenic shock, heart failure, any bleeding, and any vascular complications (85). However, another study of patients with AMI found no sex differences in the prescription of aspirin, beta-blockers, ACE inhibitors, or angiotensin receptor blockers (86). Consistent with prior studies, women were 46% less likely than men to undergo coronary angiography but had similar rates of revascularization (86). Interestingly, subacute stent thrombosis was found to be less in women compared with men (85). Women undergoing ICD insertion were more likely to have procedural complications than men (87), but effectiveness of the ICD seemed to be similar (84). Women with heart failure had similar rates of use of ACE inhibitors, angiotensin receptor blockers, beta-blockers, aldosterone inhibitors, and cardiac resynchronization therapy as men but significantly less use of ICDs, anticoagulation therapy for atrial fibrillation, and education for heart failure (88).

Although many studies have documented the existence of disparities, only a few studies have tested interventions to reduce racial and sex differences in care. Implementation of a financial reward system in the United Kingdom was associated with a larger improvement in quality of care in poor areas with a higher minority population, leading to a narrowing of the wealthy–poor (and white–nonwhite) disparity in the quality of care (37). In a study from Israel, Novack et al. (89) found that female sex was no longer a significant risk factor for mortality after implementation of the 2000 European and American guidelines for Acute Coronary Syndromes. McWilliams et al. (90) examined trends in risk factors for coronary artery disease in the U.S. from 1996 to 2000 and found that, although all racial groups improved, differences in risk factor control persisted. The one exception was for patients enrolled in Medicare, where racial differences were smaller. These studies indicate that quality improvement strategies and programs targeted at all patients can have the impact of narrowing absolute differences in care between different groups.

Reprint requests and correspondence: Dr. Mark A. Hlatky, Stanford University School of Medicine, HRP Redwood Building, Room 150, Stanford, California 94305-5405. E-mail: hlatky@stanford.edu.

REFERENCES

1. Protective Studies Collaboration. Body-mass index and cause-specific mortality in 900,000 adults: collaborative analyses of 57 prospective studies. Lancet 2009;373:1083–96.
2. Jensen MK, Chiuve SE, Rimm EB, et al. Obesity, behavioral lifestyle factors, and risk of acute coronary events. Circulation 2008;117:3062–9.
3. Wilson PWF, Bozeman SR, Burton TM, Hoaglin DC, Ben-Joseph R, Pashos CL. Prediction of first events of coronary heart disease and stroke with consideration of adiposity. Circulation 2008;118:124–30.
4. Madala MC, Franklin BA, Chen AY, et al. Obesity and age of first non–ST-segment elevation myocardial infarction. J Am Coll Cardiol 2008;52:979–85.
5. Schunkert H, Götz A, Braund P, et al. Repeated replication and a prospective meta-analysis of the association between chromosome 9p21.3 and coronary artery disease. Circulation 2008;117:1675–84.
6. Paynter NP, Chasman DI, Buring JE, Shiffman D, Cook NR, Ridker PM. Cardiovascular disease risk prediction with and without knowledge of genetic variation at chromosome 9p21.3. Ann Intern Med 2009;150:65–72.
7. Ikram MA, Seshadri S, Bis JC, et al. Genomewide association studies of stroke. N Engl J Med 2009;360:1718–28.
8. The SEARCH Collaborative Group. *SLCO1B1* variants and statin-induced myopathy—a genomewide study. N Engl J Med 2008;359:789–99.
9. The International Warfarin Pharmacogenetics Consortium. Estimation of the warfarin dose with clinical and pharmacogenetic data. N Engl J Med 2009;360:753–64.
10. Patrick AR, Avorn J, Choudhry N. Cost-effectiveness of genotype-guided warfarin dosing for patients with atrial fibrillation. Circ Cardiovasc Qual Outcomes 2009;2:429–36.
11. Eckman MH, Rosand J, Greenberg SM, Gage BF. Cost-effectiveness of using pharmacogenetic information in warfarin dosing for patients with nonvalvular atrial fibrillation. Ann Intern Med 2009;150:73–83.
12. Ridker PM, Danielson E, Fonseca FAH, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med 2008;359:2195–207.
13. Michos ED, Blumenthal RS. Prevalence of low low-density lipoprotein cholesterol with elevated high sensitivity C-reactive protein in the US. J Am Coll Cardiol 2009;53:931–5.
14. Spatz ES, Canavan ME, Desai MM. From here to JUPITER. Identifying new patients for statin therapy using data from the 1999–2004 National Health and Nutrition Examination survey. Circ Cardiovasc Qual Outcomes 2009;2:41–8.
15. Heart Protection Study Collaborative Group. Statin cost-effectiveness in the United States for people at different vascular risk levels. Circ Cardiovasc Qual Outcomes 2009;2:65–72.
16. Pletcher MJ, Lazar L, Bibbins-Domingo K, et al. Comparing impact and cost-effectiveness of primary prevention strategies for lipid-lowering. Ann Intern Med 2009;150:243–54.
17. Alsheikh-Ali AA, Trikalinos TA, Kent DM, Karas RH. Statins, low-density lipoprotein cholesterol, and risk of cancer. J Am Coll Cardiol 2008;52:1141–7.
18. Ridker PM, Danielson E, Fonseca FAH, et al. Reduction in C-reactive protein and LDL cholesterol and cardiovascular event rates after initiation of rosuvastatin: a prospective study of the JUPITER trial. Lancet 2009;373:1175–82.
19. Giraldez RR, Giugliano RP, Mohanavelu S, et al. Baseline low-density lipoprotein cholesterol is an important predictor of the benefit of intensive lipid-lowering therapy. J Am Coll Cardiol 2008;52:914–20.
20. Mauri L, Silbaugh TS, Wolf RE, et al. Long-term clinical outcomes after drug-eluting and bare-metal stenting in Massachusetts. Circulation 2008;118:1817–27.
21. Austin D, Oldroyd KG, McConnachie A, et al. Drug-eluting stents versus bare-metal stents for off-label indications. A Propensity Score-Matched Outcome Study. Circ Cardiovasc Intervent 2008;1:45–52.
22. Ryan J, Linde-Zwirble W, Engelhart L, Cooper L, Cohen DJ. Temporal changes in coronary revascularization procedures, outcomes, and costs in the bare-metal stent and drug-eluting stent eras. Results from the US Medicare program. Circulation 2009;119:952–61.
23. James SK, Stenestrand U, Lindbäck J, et al. Long-term safety and efficacy of drug-eluting versus bare-metal stents in Sweden. N Engl J Med 2009;360:1933–45.
24. Groeneveld PW, Matta MA, Greenhut AP, Yang F. Drug-eluting compared with bare-metal coronary stents among elderly patients. J Am Coll Cardiol 2008;51:2017–24.
25. Hannan EL, Racz M, Holmes DR, et al. Comparison of coronary artery stenting outcomes in the eras before and after the introduction of drug-eluting stents. Circulation 2008;117:2071–8.
26. Douglas PS, Brennan JM, Anstrom KJ, et al. Clinical effectiveness of coronary stents in elderly persons. Results from 262,700 Medicare patients in the American College of Cardiology–National Cardiovascular Data Registry. J Am Coll Cardiol 2009;53:1629–41.
27. Shishehbor MH, Goel SS, Kapadia SR, et al. Long-term impact of drug-eluting stents versus bare-metal stents on all-cause mortality. J Am Coll Cardiol 2008;52:1041–8.
28. Kaltoft A, Jensen LO, Maeng M, et al. 2-year clinical outcomes after implantation of sirolimus-eluting, paclitaxel-eluting, and bare-metal coronary stents. Results from the WDHR (Western Denmark Heart Registry). J Am Coll Cardiol 2009;53:658–64.
29. Kirtane AJ, Gupta A, Iyengar S, et al. Safety and efficacy of drug-eluting and bare metal stents. Comprehensive meta-analysis of randomized trials and observational studies. Circulation 2009;119:3198–206.
30. Weintraub WS, Boden WE, Zhang Z, et al. Cost-effectiveness of percutaneous coronary intervention in optimally treated stable coronary patients. Circ Cardiovasc Qual Outcomes 2008;1:12–20.
31. Merchant RM, Becker LB, Abella BS, Asch DA, Groeneveld PW. Cost-effectiveness of therapeutic hypothermia after cardiac arrest. Circ Cardiovasc Qual Outcomes 2009;2:421–8.
32. Hebert PL, Sisk JE, Wang JJ, et al. Cost-effectiveness of nurse-led disease management for heart failure in an ethnically diverse urban community. Ann Intern Med 2008;149:540–8.
33. Weintraub WS, Spertus JA, Kolm P, et al. Effect of PCI on quality of life in patients with stable coronary disease. N Engl J Med 2008;2008:677–87.
34. Mark DB, Pan W, Clapp-Channing NE, et al. Quality of life after late invasive therapy for occluded arteries. N Engl J Med 2009;360:774–83.
35. Mark DB, Anstrom KJ, Sun JL, et al. Quality of life with defibrillator therapy or amiodarone in heart failure. N Engl J Med 2008;359:999–1008.
36. Mark DB, Knight JD, Velazquez EJ, et al. Quality of life and economic outcomes with surgical ventricular reconstruction in ischemic heart failure: results from the Surgical Treatment for Ischemic Heart Failure trial. Am Heart J 2009;157:837–44.
37. Doshi JA, Zhu J, Lee BY, Kimmel SE, Volpp KG. Impact of a prescription copayment increase on lipid-lowering medication adherence in veterans. Circulation 2009;119:390–7.
38. Solomon MD, Goldman DP, Joyce GF, Escarce JJ. Cost sharing and the initiation of drug therapy for the chronically ill. Arch Intern Med 2009;169:740–8.
39. Volpp KG, Troxel AB, Pauly MV, et al. A randomized, controlled trial of financial incentives for smoking cessation. N Engl J Med 2009;360:699–709.
40. Doran T, Fullwood C, Kontopantelis E, Reeves D. Effect of financial incentives on inequalities in the delivery of primary clinical care in England: analysis of clinical activity indicators for the quality and outcomes framework. Lancet 2008;372:728–36.
41. Tricoci P, Allen JM, Kramer JM, Califf RM, Smith SC. Scientific evidence underlying the ACC/AHA clinical practice guidelines. JAMA 2009;301:831–41.
42. O'Connor GT, Olmstead EM, Nugent WC, et al. Appropriateness of coronary artery bypass graft surgery performed in Northern New England. J Am Coll Cardiol 2008;51:2323–8.
43. Brown PP, Kugelmass AD, Cohen DJ, et al. The frequency and cost of complications associated with coronary artery bypass grafting

surgery: results from the United States Medicare program. Ann Thorac Surg 2008;85:1980–7.
44. Baser O, Fan Z, Dimick JB, Staiger DO, Birkmeyer JD. Outlier payments for cardiac surgery and hospital quality. Health Aff 2009; 28:1154–60.
45. Shahian DM, Normand SLT. Comparison of "risk-adjusted" hospital outcomes. Circulation 2008;117:1955–63.
46. Guru V, Tu JV, Etchells E, et al. Relationship between preventability of death after coronary artery bypass graft surgery and all-cause risk-adjusted mortality rates. Circulation 2008;117:2969–76.
47. Auerbach AD, Hilton JF, Maselli J, Pekow PS, Rothberg MB, Lindenauer PK. Shop for quality or volume? Volume, quality, and outcomes of coronary artery bypass surgery. Ann Intern Med 2009; 150:696–704.
48. Kutcher MA, Klein LW, Ou FS, et al. Percutaneous coronary interventions in facilities without cardiac surgery on site: a report from the National Cardiovascular Data Registry (NCDR). J Am Coll Cardiol 2009;54:16–24.
49. Wang TY, Peterson ED, Dai D, et al. Patterns of cardiac marker surveillance after elective percutaneous coronary intervention and implications for the use of periprocedural myocardial infarction as a quality metric: a report from the National Cardiovascular Data Registry (NCDR). J Am Coll Cardiol 2008;51:2068–74.
50. Srinivas VS, Hailpern SM, Koss E, Monrad ES, Alderman MH. Effect of physician volume on the relationship between hospital volume and mortality during primary angioplasty. J Am Coll Cardiol 2009;53:574–9.
51. Ho PM, Magid DJ, Shetterly SM, et al. Medication nonadherence is associated with a broad range of adverse outcomes in patients with coronary artery disease. Am Heart J 2008;155:772–9.
52. Daskalopoulou SS, Delaney JA, Filion KB, Brophy JM, Mayo NE, Suissa S. Discontinuation of statin therapy following an acute myocardial infarction: a population-based study. Eur Heart J 2008 July 29 [E-pub ahead of print].
53. Shalev V, Chodick G, Silber H, Kokia E, Jan J, Heymann AD. Continuation of statin treatment and all-cause mortality. A population-based cohort study. Arch Intern Med 2009;169:260–8.
54. Dormuth CR, Patrick AR, Shrank WH, et al. Statin adherence and risk of accidents. A cautionary tale. Circulation 2009;119:2051–7.
55. Heisler M, Hogan MM, Hofer TP, Schmittdiel JA, Pladevall M, Kerr EA. When more is not better: treatment intensification among hypertensive patients with poor medication adherence. Circulation 2008;117:2884–92.
56. Gibson CM, Pride YB, Frederick PD, et al. Trends in reperfusion strategies, door-to-needle and door-to-balloon times, and in-hospital mortality among patients with ST-segment elevation myocardial infarction enrolled in the National Registry of Myocardial Infarction from 1990 to 2006. Am Heart J 2008;156:1035–44.
57. Mehta RH, Bufalino VJ, Pan W, et al. Achieving rapid reperfusion with primary percutaneous coronary intervention remains a challenge: insights from American Heart Association's Get With The Guidelines program. Am Heart J 2008;155:1059–67.
58. Ting HH, Bradley EH, Wang Y, et al. Delay in presentation and reperfusion therapy in ST-elevation myocardial infarction. Am J Med 2008;121:316–23.
59. Dorsch MF, Greenwood JP, Priestley C, et al. Direct ambulance admission to the cardiac catheterization laboratory significantly reduces door-to-balloon times in primary percutaneous coronary intervention. Am Heart J 2008;155:1054–8.
60. Devlin G, Gore JM, Elliott J, et al. Management and 6-month outcomes in elderly and very elderly patients with high-risk non–ST-elevation acute coronary syndromes: the Global Registry of Acute Coronary Events. Eur Heart J 2008;29:1275–82.
61. Forman DE, Cannon CP, Hernandez AF, Liang L, Yancy C, Fonarow GC. Influence of age on the management of heart failure: findings from Get With The Guidelines-Heart Failure (GWTG-HF). Am Heart J 2009;157:1010–7.
62. Piccini JP, Hernandez AF, Dai D, et al. Use of cardiac resynchronization therapy in patients hospitalized with heart failure. Circulation 2008;118:926–33.
63. Schiele F, Meneveau N, Seronde MF, et al. Changes in management of elderly patients with myocardial infarction. Eur Heart J 2009;30: 987–94.
64. Chen JL, Sosnov J, Lessard D, Goldberg RJ. Impact of do-not resuscitation orders on quality of care performance measures in patients hospitalized with acute heart failure. Am Heart J 2008;156: 78–84.
65. Jneid H, Fonarow GC, Cannon CP, et al. Impact of time of presentation on the care and outcomes of acute myocardial infarction. Circulation 2008;117:2502–9.
66. Aujestky D, Jimenez D, Mor MK, Geng M, Fine MJ, Ibrahim SA. Weekend versus weekday admission and mortality after acute pulmonary embolism. Circulation 2009;119:962–8.
67. Lee DS, Tu JV, Chong A, Alter DA. Patient satisfaction and its relationship with quality and outcomes of care after acute myocardial infarction. Circulation 2008;118:1938–45.
68. Curtis JP, Luebbert JJ, Wang Y, et al. Association of physician certification and outcomes among patients receiving an implantable cardioverter-defibrillator. JAMA 2009;301:1661–70.
69. Karamlou T, Diggs BS, Person T, Ungerleider RM, Welke KF. National practice patterns for management of adult congenital heart disease: operation by pediatric heart surgeons decreases in-hospital death. Circulation 2008;118:2345–52.
70. Schwamm LH, Fonarow GC, Reeves MJ, et al. Get With The Guidelines–stroke is associated with sustained improvement in care for patients hospitalized with acute stroke or transient ischemic attack. Circulation 2009;119:107–15.
71. Brush JE, Rensing E, Song F, et al. A statewide collaborative initiative to improve the quality of care for patients with acute myocardial infarction and heart failure. Circulation 2009;119:1609–15.
72. Piazza G, Rosenbaum EJ, Pendergast W, et al. Physician alerts to prevent symptomatic venous thromboembolism in hospitalized patients. Circulation 2009;119:2196–201.
73. Peikes D, Chen A, Schore J, Brown R. Effects of care coordination on hospitalization, quality of care, and health care expenditures among Medicare beneficiaries. 15 randomized trials. JAMA 2009;301:603–18.
74. Auer R, Gaume J, Rodondi N, Cornuz J, Ghali WA. Efficacy of in-hospital multidimensional interventions of secondary prevention after acute coronary syndrome: a systematic review and meta-analysis. Circulation 2008;117:3109–17.
75. Bibbins-Domingo K, Pletcher MJ, Lin F, et al. Racial differences in incident heart failure among young adults. N Engl J Med 2009;360: 1179–90.
76. Shaw LJ, Shaw RE, Merz CN, et al. Impact of ethnicity and gender differences on angiographic coronary artery disease prevalence and in-hospital mortality in the American College of Cardiology–National Cardiovascular Data Registry. Circulation 2008;117:1787–801.
77. Cook NL, Ayanian JZ, Orav EJ, Hicks LS. Differences in specialist consultations for cardiovascular disease by race, ethnicity, gender, insurance status, and site of primary care. Circulation 2009;119:2463–70.
78. Xie J, Wu EQ, Zheng ZJ, Sullivan PW, Zhan L, Labarthe DR. Patient-reported health status in coronary heart disease in the United States: age, sex, racial, and ethnic differences. Circulation 2008;118: 491–7.
79. Yancy CW, Abraham WT, Albert NM, et al. Quality of care of and outcomes for African Americans hospitalized with heart failure: findings from the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure) registry. J Am Coll Cardiol 2008;51:1675–84.
80. Waldman SV, Blumenthal JA, Babyak MA, et al. Ethnic differences in the treatment of depression in patients with ischemic heart disease. Am Heart J 2009;157:77–83.
81. Wellenius GA, Mittleman MA. Disparities in myocardial infarction case fatality rates among the elderly: the 20-year Medicare experience. Am Heart J 2008;156:483–90.
82. Spertus JA, Jones PG, Masoudi FA, Rumsfeld JS, Krumholz HM. Factors associated with racial differences in myocardial infarction outcomes. Ann Intern Med 2009;150:314–24.
83. Auble TE, Hsieh M, Yealy DM. Differences in initial severity of illness between black and white emergency department patients hospitalized with heart failure. Am Heart J 2009;157:306–11.
84. Albert CM, Quigg R, Saba S, et al. Sex differences in outcome after implantable cardioverter defibrillator implantation in nonischemic cardiomyopathy. Am Heart J 2008;156:367–72.

85. Holman RR, Paul SK, Bethel A, Matthews DR, Neil HAW. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008;359:1577–89.
86. Nguyen JT, Berger AK, Duval S, Luepker RV. Gender disparity in cardiac procedures and medication use for acute myocardial infarction. Am Heart J 2008;155:862–8.
87. Peterson PN, Daugherty SL, Wang Y, et al. Gender differences in procedure-related adverse events in patients receiving implantable cardioverter-defibrillator therapy. Circulation 2009;119:1078–84.
88. Yancy CW, Fonarow GC, Albert NM, et al. Influence of patient age and sex on delivery of guideline-recommended heart failure care in the outpatient cardiology practice setting: findings from IMPROVE HF. Am Heart J 2009;157:754–62.
89. Novack V, Cutlip DE, Jotkowitz A, Lieberman N, Porath A. Reduction in sex-based mortality difference with implementation of new cardiology guidelines. Am J Med 2008;121:597–603.
90. McWilliams JM, Meara E, Zaslavsky AM, Ayanian JZ. Differences in control of cardiovascular disease and diabetes by race, ethnicity, and education: US trends from 1999 to 2006 and effects of Medicare coverage. Ann Intern Med 2009;150:505–15.

Key Words: epidemiology ■ health services research ■ outcomes.